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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/897,801	06/29/2001	Thomas C. Pinkerton	24967/USA 0367/1/US (6794	1264

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EXAMINER	
HAYES, MICHAEL J	

ART UNIT	PAPER NUMBER
3767	

DATE MAILED: 12/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/897,801	PINKERTON, THOMAS C.	
	Examiner	Art Unit	
	Michael J. Hayes	3767	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 85,87-92,94-97,99-102,105-108,110-113,116,119,121-126,128,129,131-136 and 138-145.

Continuation of Disposition of Claims: Claims rejected are 85,87-92,94-97,99-102,105-108,110-113,116,119,121-126,128,129,131-136 and 138-145.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 139-145 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is no description of ratio of Cmax produced by dermis administration to that produced by subcutaneous administration of at least 2.2. There is no description for an unlimited upper limit of the ratio and no description for other than genotropin administered by a single needle (as shown in Table 3 of Example XII). There is no description for tmax by dermal administration compared to tmax subcutaneous administration in the range 0-38%. There is no description for the ratio range to be extremely small (i.e., close to 0%) and the only description in the neighborhood of 38% is for Almotriptan administered intradermally with a 6 needle array, as shown in Table 3 of Example XII. There is no description of using dalteparin as recited in claim 142. If Applicant is describing dalteparin as a generic name for Fragmin (as opposed to Fibrin), then evidence should be provided.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 85, 87-91, 94-97, 99, 100, 101, 105-108, 110, 111, 112, 116, 119, 121-125, 128, 129, 131-135, 138, and 139-145 are rejected under 35 U.S.C. 103(a) as being unpatentable over GROSS in view of D'Antonio et al. (US Patent No. 6,056,716) or Puri et al. (*An Investigation Of The Intradermal Route As An Effective Means Of Immunization For Microparticulate Vaccine Delivery Systems*, Vaccine 18 (2000) 2600-2612).

If the method disclosed by Gross does not inherently show improved systemic absorption relative to absorption produced upon subcutaneous bolus administration, it would have been obvious to one of ordinary skill in the art to modify the method to obtain improved systemic absorption relative to absorption produced upon subcutaneous bolus administration. Gross discloses a method of delivering various drugs and medicine, including heparin and somatotropin (growth hormone) intradermally (3:40-41) using a single needle with an outlet at a depth of 250 gm - 2mm in a controlled manner based on needle diameter (4:10-35). Gross discloses that the delivery can be pulsatile (i.e., repeated bolus injections). Upon delivering medication to the intradermal compartment, the physiology of this location causes the improved systemic absorption as compared to bolus subcutaneous injections. D'Antonio and Puri disclose that medication delivered intradermally results in improved systemic absorption. D'Antonio (3:27-

28, 29:3-26) teaches ID injections for growth hormones, vaccines, sera, vitamins, and nutrients. D'Antonio discloses that intradermal injection testing shows a better absorption than subcutaneous injection as evidenced by tests showing that ID is more potent than subcutaneous injections. Puri teaches better absorption by ID injections for microparticulate vaccines having better absorption than subcutaneous injections as evidenced by lower required doses when administered ID (See abstract, pg. 2601, 2607-2610). It would have been obvious to one of ordinary skill in the art at the time of the invention to use the teachings of D'Antonio and/or Puri in the method of Gross in order to achieve a therapeutic result using less drugs. The cost savings and ability to effectively deliver scarce drugs to a larger number of people would motivate one of ordinary skill in the art to modify the method of Gross with the teachings of D'Antonio and/or Puri.

The use of nanoparticles are considered as equivalent to the disclosed use of microparticles in the prior art, and obvious to give improved absorption, particularly in consideration that the nanoparticles are even smaller than the microparticles. Additionally, in view of the large number and classes of drugs listed by Gross for delivery by the disclosed method, the use of dopamine receptor agonist would have been obvious to one of ordinary skill in the art because it is recognized as another similar drug. One of ordinary skill in the art would have the knowledge to apply the disclosed method to additional drugs.

Re claims 139-141 and 143-145 D'Antonio teaches that injections into the dermis as many times more potent than subcutaneous injections. It would have been obvious to one of ordinary skill in the art at the time of the invention that these teachings of D'Antonio would encompass Cmax ratios greater that 2.2 and tmax ratios less than 38% of intradermal to

subcutaneous parameters. One of ordinary skill in the art would recognize that Cmax and tmax are common parameters addressing the potency of injections and the teaching of many multiples of increased potency would encompass the claimed ranges.

Re claim 142 the use of a type of heparin as the agent to administer would have been obvious to one of ordinary skill in the art at the time of the invention because administering various types of heparin would be known in view of the disclosure of Gross to administer heparin.

Claims 92, 102, 113, 126, and 136 are rejected under 35 U.S.C. 103(a) as being unpatentable over GROSS in view of D'ANTONIO or PURI as applied to claims 91, 97, 107, 125, or 135 above, and further in view of GANDERTON et al. (US Patent No. 3,8 14,097). Gross discloses the claimed method except for using an array of needles. Ganderton discloses injecting a substance through multiple needles (1:9-40). See fig. 1. It would have been obvious to one of ordinary skill in the art at the time of the invention to use the teachings of Ganderton in the method of Gross and D'Antonio or Puri in order to facilitate the distribution of delivered drug to a patient.

Response to Arguments

Applicant argues that Gross does not disclose bolus injections because Gross states the injections are to be performed slowly. Applicant has not established any parameters with respect to the interpretation of the term "slowly" and it appears that Applicant regards use of the term to require infusion. The examiner does not agree because a bolus injection may be performed slowly. Though a bolus injection is understood to occur more quickly than infusion of fluid, a

bolus injection can be administered over a range of time. Since there is a range of time over which to administer a bolus injection, the administration may be slowly (at the high end of the range) or slowly (at the low end of the range). Gross discloses pulsatile administration of a drug that would constitute repeated bolus administration, as opposed to continuous infusion of a drug.

Applicant generally argues that D'Antonio and Puri are not concerned with the administration of heparin, but rather the injection of vaccines and therefore fail to provide motivation to modify the method disclosed by Gross. The examiner maintains the rejections because Puri and D'Antonio are concerned with the same problem confronted with Gross, that is, methods administering drugs (i.e., body affecting agents) and how to best deliver an agent to a patient. The prior art discusses better absorption of drugs when administered intradermally as compared to subcutaneously and provide the required motivation to deliver the drugs in this manner.

Applicant argues that Ganderton does not disclose bolus intradermal administration of heparin and does not resolve the deficiencies of the prior art in disclosing the claimed limitations. The examiner maintains the rejection because Ganderton was relied upon to show administration of drugs using an array of needles.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Hayes at (571) 272-4959. The examiner can usually be reached Monday -Thursday, 7:00-4:30, and on alternate Fridays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kevin Sirmons, can be contacted at (571) 272-4965. The fax number for submitting official papers is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

mjh
11 December 2005

MICHAEL J. HAYES
PRIMARY EXAMINER